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THE NECESSITY FOR A NEW STANDPOINT IN SLEEP THEORIES.

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Sleep theories have suffered from two great lacks, lack of community of work and lack of systematization. Although many valuable researches have been made upon the physiological conditions of sleep, the work so far has been scattered and carried on, for the most part, by specialists in their own departments, without a proper realization of the breadth of the problem or the interrelation of its various phases. Recent theories have shown a tendency to combine elements from the three main lines of investigation followed, but such systematization has not been carried far. It is the object of the present article to subject the factual basis of the vasomotor, the chemical, and the histological theories of sleep to as thoroughgoing and impartial criticism as possible, and to show the exact relation of each to the problem in hand. In attempting this it has been necessary to treat the subject from the evolutionary standpoint. The theory presented in the concluding chapter claims nothing of finality. It is not our purpose to add another to the already too numerous theories of sleep, but rather to gain a new point of attack,—which we believe to be the only point of attack that offers promise of a solution of the problem.

I. THE CIRCULATION THEORIES.

The phenomenon of sleep has never received the attention that, from its importance to life, it deserves. As with all scientific problems which have been of general interest to mankind,

the first explanations were attempted by the philosophers. Kant[1] marks an important epoch in sleep theories, since he definitely turns these problems over to science, declaring that physiologists alone are capable of formulating a satisfactory theory. To the earlier physiologists, explanations in terms of animal spirits, nervous fluid, cerebral vibrations, etc., were very easy. Sleep was commonly explained as due to the exhaustion of the nervous fluid or to a diminution in its mobility. During this period it was supposed to flow back to the brain and nervous centers. When the nervous system was sufficiently recharged and the recuperated muscles ready to respond, awakening resulted.[2]

With the advent of a more scientific physiology in the first quarter of the present century, vitalism was gradually forced to retire, but in sleep theories many of the elements that were closely associated with the older theories remained. Albrecht von Haller and Hartley, in particular, had insisted on the part that the circulation of the blood plays in the causation of sleep. Sleep was for them the result of pressure on the brain due to venous congestion, which impeded the flow of the nervous fluid or interfered with the cerebral vibrations. They also adduced many facts and observations in support of venous congestion. Subsequent investigators contributed still more, until quite an imposing structure was reared. Until 1870, this congestion theory in one form or another was that most widely accepted. The chief observations on which it rests are:

1. The resemblance of sleep to apoplexy, epileptic seizures, and allied pathological states, in which there is a clearly marked congestion.
2. Pressure on the brain produces unconsciousness in cases of fractured skull.
3. The horizontal position (and according to some authors, the head lower than trunk) is favorable to sleep.
4. Children and the aged (?) sleep more than the normal adult. This in the case of children was interpreted as due to compression of the skull upon the growing brain, in the aged, to loss of tone of cerebral vessels. For lack of compression, the sympathetic system never sleeps. Full blooded people are good sleepers.
5. Opiates and narcotics induce sleep by derivation of the blood to the head. (?)
6. 'All the causes which tend to produce sleep are causes that tend to lower the action of the heart or to retard the circulation in the brain' and hence to bring about a state of cerebral congestion. (?)[3]

In general criticism, it need only be said that this theory is now absolutely contradicted by experimental evidence, and

[1] Kant: p. 126.

[2] For historical résumés of sleep theories, see Duval (Jacoud), Ch. Pupin, Radestock (appendix). For the Vitalistic theories, see Hartley, Haller, Erasmus Darwin, Clutterbach, Hammond (1869), and Encl. Brit. (1799).

[3] Many of these observations are palpably incorrect.

serves as a warning of the danger of attempting an explanation of a physiological state by reference to a pathological state that bears to it only superficial resemblances.[1]

The next theory to gain general ground was still a theory in terms of blood circulation, but was directly opposed to the preceding, in that it attributed sleep to cerebral anæmia. Before attempting any general statement or criticism, we shall first treat of its history. Blumenbach,[2] in 1795, advocated the diminution of the circulation of the blood as the proximate cause of sleep. His conclusion was based upon an observation on the volume of the brain in a young man who had fractured his skull by a fall. The opening remained covered only by the membrane. During sleep the chasm was deep, in waking hours superficial. In 1821, a case of fractured skull in a Montpellier woman was reported,[3] and later another case by Kennedy, confirming Blumenbach's observations.[4] The first attempt at experimentation was made by Donders (1854), who cut away a piece of the skull of an animal and examined the condition of the cerebral vessels through a watch glass cemented over the hiatus. He discovered the condition to be that of anæmia. Kussmaul and Tenmer in Germany repeated the experiment. In 1855, Fleming reported that the compression of the carotid arteries on himself and other subjects produced a dreamlike state of consciousness, while compression of the jugular veins resulted in an entirely different state.

So far these experiments and observations were scattered and had not attracted general attention, yet together with the other objections that could be urged, they were sufficient, in many quarters, to shake confidence in the congestion theory. A few of the writers who treat sleep at all were favorably impressed with anæmia, while many others grew non-committal. The time was now ripe for the more thorough and convincing investigations of Durham and Hammond. As has frequently happened in the history of science, these experiments were carried on independently and almost at the same time. Durham was the first to publish. His monograph on the Physiology of Sleep marks the beginning of a new epoch in the study of sleep problems. It justly deserves to rank as a classic.

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[1] With this theory can be associated such names as Cabanis, Bedford-Brown, G. H. Lewes, Metcalfe, H. Holland, Marshall Hall, Clutterbach, Sieveking, Dickson, Macnish, and W. B. Carpenter (in his earlier writings).

[2] Bluemenbach: (Tr.) p. 199.

[3] According to Durham the Montpellier case was reported by Caldwell, according to Hammond by Dendy. I have not been able to find the original.

[4] For other cases of fractured skull see Brown, Hammond (1869), Mosso (1880).

His experiments were performed chiefly on dogs. After chloroforming, a portion of the skull about the size of a shilling was removed by trephining from the parietal region and the dura mater cut away.[1] Durham found a remarkable contrast in the appearance of the brain during its periods of rest and activity. In the former state, veins, capillaries, and smaller arteries were indistinct, and the surface pale and below the level of the bone, while in the latter the vessels were filled with blood, clearly distinguishable in color, and the surface was distended and rosy. In order to satisfy himself still further as to the value of his experiments, he used the watch glass precaution for excluding the influence of atmospheric pressure, applied powerful lenses, and compared the cerebral condition of waking and sleeping dogs placed side by side. Later, by artificial ligaturing of carotids and jugulars, he confirmed Fleming's observations.

Rejecting the congestion theory, he attempts to formulate a theory of his own. His fundamental standpoint is seen in the definition of sleep as "that particular state of cerebral inactivity, which is essentially associated with nutrition and repair of brain substance." Now, according to Durham, cerebral inactivity is directly proportional to oxidation of brain substance. Consequently, whatever tends to lessen the mutual affinity of brain tissue and oxygen or to prevent that affinity from coming into active operation, may, within certain limits, become more or less directly the cause of sleep. Among such causes, he enumerates the diminished susceptibility of the brain matter itself, the diminished activity of the oxygen supplied, and the accumulation of decomposition-products which catalytically check the reaction. It is upon the last mentioned cause that Durham lays most stress. But none of these causes can come into decisive operation unless the requisite state of circulation can be established. The conditions of circulation usually obtaining during sleep are both peculiarly favorable and necessary to extensive nutrition.[2] The oxygen supply depends upon the state of cerebral circulation and this in turn is in a relation of direct mutual interdependence to the condition of the brain. Therefore, powerful predisposing causes to sleep may be found in whatever tends to decrease cerebral circulation. This decrease can be brought about either through the nervous system, *e. g.*, by presence or absence of stimuli,

[1] Durham: 1860, pp. 153 ff.

[2] During activity, the rapid and abundant flow of blood through the capillaries results in a large supply of oxygen, favors endosmosis into the vessels of products of oxidation, and is unfavorable to exosmosis of nutriment material from vessel to tissue. During sleep, the slower and diminished flow of blood favors exosmosis. *Vide* Kohlschütter (1869).

central or peripheral, or through the vascular system, *e. g.*, by decrease in force or frequency of heart beat.

Durham deserves much credit for the wide range of facts on which he bases his conclusions and for his scientific caution; but it is evident that his theory does not go far towards an explanation of sleep. It is fairly bristling with special problems, and is made up of elements that call for greater systematization and subordination. Traces of three more or less distinct lines, which investigators have subsequently followed, are visible: (1) the effects of auto-intoxication, (2) the necessity of oxygen to cerebral activity, and (3) the study of the mechanism by which the vascular changes are brought about. The first two tend to theories which emphasize chemical activities and reduce alterations in circulation to the role of a secondary factor. Hence we shall postpone consideration of the auto-intoxication, and a general discussion of the necessity of oxygen, until we come to treat of the chemical theories. An important point to notice about Durham's theory, and one that has been generally overlooked, is that he never definitely commits himself to more than the statement of a mutual interdependence of the condition of the brain and the condition of the circulation. He does not state whether cerebral anæmia is the cause or a result of cerebral inactivity.

Wm. Hammond's attention was first directed to the anæmic condition of the brain during sleep by a case of fractured skull in 1854.[1] His experiments (1860) were of the same character as Durham's, although not as extensive except upon the influence of anæsthetics and narcotics on the circulation. They yielded like results.[2] Later by means of a manometer he conclusively demonstrated that the blood pressure on the brain is less during sleep.[3] Hammond makes little attempt at theory. After pointing out the chief differences between sleep and stupor, he attributes the exciting cause of sleep to the necessity for nutrition and the removal of waste, the immediate cause to cerebral anæmia. This influence of anæmia is shown by the action of the heart, which draws the blood from the internal organs, including the brain, to the skin, thus causing sleepiness; by the action of extreme cold, which produces similar effects; by the action of digestion, which draws the blood to the alimentary tract; and by the tendency to sleep as exhibited in debility and excessive

[1] For Hammond's works, see Bibliog. at end.

[2] For other experiments, see Vizioli, Mosso (1880). Tarchanoff (1894) has recently by experiments on young puppies entirely eliminated the possible factor of chloroformization.

[3] Hammond (1869), appendix. Weir Mitchell's experiments confirm.

loss of blood. Although unelaborated, this is a clear statement of the vasomotor theory.[1]

Investigators of sleep phenomena now became more numerous. Their work, however, was still characterized by little community of labor. It will hardly be profitable to treat of all the investigations and all the theories of the vasomotor type in chronological order. We shall content ourselves, therefore, with picking out a few of the most typical.

Girondeau (1868), making use of the discovery by Boll and Robin of the lymphatic spaces around the cerebral vessels, attempted, in a rather fantastic fashion, to account for the retardation of the blood circulation by a compression of the vessels due to an accumulation of lymph. J. Leonard Corning (1882), in studying the connection of throbbing carotids with epileptic attacks, invented an instrument for carotid compression. Through its means, he found that a certain degree of compression in the evening was much more efficient in the production of sleep than in the morning. Arguing from this fact to the conclusion that the flow of oxygenated blood was in each case the same, he is led to seek the primary impulse to sleep in the exhaustion of stored intra-ganglionic material. The continuance of function depends upon the amount of this material. But there is another physiological factor, which, although following in time, is of equal importance with the first. The explosion of plastic material is immediately dependent upon the circulation which brings the oxygen supply. Other things equal, intensity of function is in the ratio of the blood supply. Corning thus correlates the two factors of exhaustion and anæmia.

A distinct advance towards a closer grappling with the problem can be seen in the work of C. A. Moore (1871). He attempts to account for the onset of sleep by a discharge of stimulating influence from certain ganglia of the sympathetic system in the neck along the vasomotor nerves of the cerebral arteries. This discharge occurs when the cerebro-spinal system, through fatigue of the brain, is no longer capable of inhibiting the sympathetic ganglia. Its effect is the reduction of the blood supply below the amount necessary to maintain functional activity, but not below the amount necessary for nutrition. Moore's theory is open to objections that make it at present untenable. Its refutation, however, is important in closing two possible lines of explanation that might be attempted. (1)[2] There is no such inherent antagonism between

[1] I shall employ the more usual term vasomotor, from the most typical in the group, in place of anæmia theory.

[2] See Porter: Donaldson. The experiments of Franck, 1894, p. 721, and of Goltz and Ewald, 1896, p. 389, are to the point.

the cerebro-spinal and sympathetic as Moore assumes; (2)[1] although high authorities have been led to believe in a special vasomotor system in the brain, the weight of scientific opinion at present is against any such system. But, however this problem may be settled, we have the strongest kind of experimental evidence that both the total amount of blood in the brain and the rapidity of flow depend chiefly upon conditions of general blood pressure.[2] Until that evidence is shaken, the probabilities are all in favor of a vasomotor theory that explains cerebral anæmia by a loss of tone in vasomotor centers. Such a theory is that of Howell (1897). It is the most recent and by far the strongest presentation of the vasomotor theory yet made. As such, it demands detailed criticism.

Howell's point of attack is gained from experiments performed on the dilatation of cutaneous vessels during sleep. A water plethysmograph was attached to the forearm of the sleeper, with the no-pressure point kept at the middle part of the portion immersed. Great difficulty was at first found in sleeping under such unusual conditions, and it was necessary, to gain satisfactory results, for the subject to fatigue himself by considerable out-of-door exercise or by light sleep on the previous night. The experimenter kept a record of the various conditions of the sleeper, and their effect on the curve. As soon as the subject lay in bed and attempted to go to sleep, the experiment began. The curve fell—the exact moment of the setting in of sleep was impossible to determine—until it reached its minimum in one to one and one-half hours, where it remained with minor oscillations for an hour or two. A quite gradual rise now commenced, growing more rapid for the half hour just preceding complete awakening. Besides the general course of the curve, there were two classes of oscillations noted: (1) short, brief, variable oscillations usually traceable to external stimuli or movements, (2) nearly hourly periodic waves probably due to rhythmic changes in the vasomotor center. Howell's experiments number twenty in all. Mosso has also made observations proving an increase in the volume of the lower limbs during sleep and a corresponding decrease during mental activity,—results which, before Howell, were confirmed by Bardeen and Nicols, and by Dr. Shields in the Johns Hopkins laboratory. Durham can be quoted in favor of dilatation of the skin vessels. He based his conclusion chiefly upon the increase of temperature at the surface, which can be seen even by the unscientific observer in the flushed condition of the skin, and upon the observations of Sanctonus, Keill and Edwards, which

[1] Foster, 5th Ed. Pt. III, pp. 1131 ff. Also, Pt. III, 1897. Mosso.
[2] Hill: 1896, pp. 40 ff.

establish that perspiration in sleep is at once more copious and solid than in the waking state. Innumerable observations in daily life go to show a reciprocal relation between the blood supply of the brain and skin. There can be no doubt of the fact of dilatation of cutaneous vessels during sleep. As to splanchnic dilatation, Howell, while admitting that it would perform the same function as cutaneous dilatation and would greatly aid in the production of cerebral anæmia, is inclined to deny it a place on the ground of lack of evidence. However, many of the highest authorities assign to the splanchnic vasomotor center the main role in the regulation of the cerebral circulation.[1] Hill's experiments show the absolute necessity, as well as the nicety of adjustment, of the splanchnic vasomotor mechanism for compensation of alterations in hydrostatic pressure due to changes of bodily position.[2] By paralysis or section of splanchnic vasoconstrictor nerves, death may follow from cerebral anæmia. The blood supply to the internal organs is not increased, for there is a noticeable decrease in function in all cases. Reciprocal relations of blood supply seem to hold here between skin and internal organs, as well as between skin and brain.

Taking the facts from his experiments as data, Howell proceeds to construct his sleep theory.[3] The derivation of blood to the skin vessels must necessarily result in a lessening of arterial pressure in the arteries at the base of the brain, thereby bringing about a condition of cerebral anæmia. If we seek the cause of this alteration of circulation, we must look to the vasomotor center. This, we know, is kept in a constant state of activity by the continual stream of in-coming and out-going impulses. That it is subject to fatigue can be shown by experiments upon the stimulation of the sciatic nerve in curarized and narcotized animals. Being thus placed at the very center of nervous activity, exposed to continual stimulation, a condition of fatigue, proportional to nervous activity, must necessarily result. Further, the long duration of sleep, after the cortical cells have regained their irritability sufficiently for arousal on moderate or slight stimulation, as shown by the curve of intensity of sleep (Kohlschütter, Michelson, and others), can best be explained by the necessity for longer rest of the vasomotor mechanism. The periodicity of sleep is, therefore, to be directly associated with the fatigue rhythm of the vasomotor cells. The lessening of the blood supply, while the immediate cause and under normal circumstances not only the necessary but the determining element, is not the only factor

[1] Foster: *op. cit.*; Porter: *op. cit.*
[2] Hill (1896): pp. 78 ff.
[3] In summarizing, I quote and abbreviate freely.

involved in the production of sleep. Two other factors, singly or together, may co-operate with anæmia: (1) a diminution of irritability, caused by fatigue of large portions of the cortical area (particularly sensory and association areas); and (2) voluntary withdrawal of sensory and mental stimuli, involved in preparation for sleep. For lack of experimental data, Howell refuses to add, as Durham and Corning did, chemical elements to his theory, or to discuss the exact relation of blood supply to functional activity or quiescence of the organ. His theory is by far the strongest presentation of the vasomotor theory yet made.

The main point of criticism is the importance attached by this theory to the fatigue of the vasomotor centers. There are two lines of attack. (1) The plethysmographic curve commenced to fall as soon as the subject assumed a horizontal position in bed and attempted to go to sleep. The curve for arterial pressure shows a similar fall under the same conditions. But these results need not be interpreted to be due wholly to loss of tone of the vasomotor cells of the bulb, for such a fall occurs whenever the subject assumes the conditions of rest. In Hill's experiments, the arterial pressure was as low in the waking state, when the subject lay in bed in the morning, as in the sleeping state in the evening. The horizontal position tends always to lower arterial pressure.[1] The absence of movement in the limbs also contributes to the same result, since it removes two important factors (the compression of the muscles and changes in position) in the return of the blood through the veins. These considerations emphasize the importance of purely mechanical and reflex causes in the circulatory changes of sleep. (2) A decrease in tone undoubtedly occurs in the vasomotor center,[2] but this loss of tone is by no means confined to that center. The other bulbar and spinal centers share it in common.[3] All reflexes are slow and less intensive.[4] At the periphery the decrease can be seen in the perceptions of dullness in the forehead and eye-lids, tingling in the conjunctiva, feeling of feebleness in the voluntary muscles, etc., which often precede sleep.[5] The nerves alone remain unaffected in their capacity for functioning.[6] The condition of the vasomotor center is, then, only one manifestation of a phenomenon, general throughout the nervous system. A search for the causes of this phenomenon leads to a general discussion of organic

[1] Hill: Lancet (1898), Jour. of Physiol. (1898). I can see no way of reconciling Hill's A. M. results with Howell's.

[2] Conclusively demonstrated by Patrizi, 1897.

[3] Manacéïne: pp. 20 ff.

[4] *Cf.* Lombard's knee-jerk experiments, 1887.

[5] Berger and Loewy.

[6] Bowditch (1890) has established the fact that nerves can function indefinitely.

rhythms, and of the relative importance of central and peripheral fatigue to the integrity of the nervous system. By the same evolutionary sanction that has given the nervous tissue control over the metabolism of all other tissues, the higher brain centers have gained domination over the periphery.[1] The cortical cells are chemically the most complex in the body.[2] The demands placed upon them for the maintenance of consciousness are heavy and irregular. While we may not exclude fatigue of the periphery as a possible factor, it is surely much more true to the known facts to look to fatigue of the higher centers and the necessity for their recuperation as the main determining element both in the time of occurrence and the duration of sleep. The initial loss of tone in the vasomotor center would then be chiefly traceable not to a local fatigue, but to Howell's two secondary factors, diminution in cortical irritability and withdrawal of stimuli. The divergence of the intensity curve of sleep and the plethysmographic curve is as readily explainable from this standpoint as from Howell's. The long continuance of sleep at low intensity would be due to the need for extensive storing of material within the cell to meet the demands of the day period, while the character of the plethysmographic curve would be accounted for by the continuance of the bodily conditions of rest, together with the low state of cortical activity and the lack of external stimuli.

From the time of Durham, circulation theories have taken as their foundation cerebral anæmia. There is another class of theories, however, which, while recognizing the force of the new experiments, has managed to save some of the elements of the older congestion theory. Sergouyef,[3] influenced largely by the definition of sleep as a state in which active nutrition is maintained without diminution, accepted anæmia of the cortex, but believed in hyperæmia of the portions at the base of the brain. His position is somewhat strengthened by Brown-Sequard, who reports observations of hyperæmia at the base of the brain in many animals during sleep, and has also shown that congestion can be produced in the same way as cerebral anæmia by bilateral section of the two great sympathetics. De Boeck and Verhoogen have more recently attempted a somewhat similar theory. According to them, the resistance to the flow of blood in the arteries supplying the cortex is greater than in those supplying the base of the brain, since they are smaller, longer and more tortuous, while the other arteries, shorter and more numerous, leave the Circle of Willis

[1] *Cf.* Verworn, p. 572.
[2] Fish: p. 109.
[3] See Berger and Loewy.

at right angles. For this reason, when the arterial pressure is lowered, anæmia in the cortex is relatively greater than in the basal ganglia. This, as Howell points out,[1] would serve to explain how functional activity of the cortex could be suspended upon moderate fall of pressure, while that of the lower centers remains. There is, however, danger in over-estimating this difference, for we have the best of reasons for believing that the activities of nutrition are not absolutely heightened, but only relatively, in proportion to tissue waste. We have shown above that the loss of tone in the nervous system is general. Owing to his peculiar mechanics of circulation, Cappie, originally a full fledged congestionist, is still able to maintain venous pressure upon the brain substance as the immediate cause of sleep.[2] He accepts the Monro-Kellie doctrine that the total quantity of blood in the cranium, since it is a closed cavity, is invariable, and that only changes in its distribution can occur.[3] Hence, arterial and capillary anæmia is to be correlated with venous congestion. Granting that the Monro-Kellie hypothesis is true, still the compression of the brain substance could not occur: for under physiological conditions the intracranial pressure (the pressure of the brain upon the cranium) and the cerebral venous pressure are the same. The brain substance transmits pressure. It, itself, is incompressible.[4]

Now that we have examined the most typical, we are ready for a summary of the principal evidence upon which the vasomotor theories rest, and a consideration of the adequacy of any such theory to cover the facts. (1) Observations made upon the condition of the brain in cases of fractured skull, show a decrease in brain volume during sleep, and mental inactivity, an increase during periods of activity and excitement. This has been confirmed by experiments with the manometer. (2) Observations upon the condition of the cerebral blood vessels, after artificially exposing with all due caution portions of the brain surface, have uniformly shown an anæmia in arteries and capillaries. (3) Experiments in carotid compression, when not carried beyond certain limits, have produced states most similar to sleep, while jugular compression has resulted in a comatose state, utterly dissimilar. (4) In cases of fracture at the base of the skull or of traumatic injury to the cribiform plate of the ethnoid bone, permitting the escape

[1] Howell: 1897, p. 340.
[2] For Cappie's works, see Bibliog.
[3] Hill, 1896, p. 30, without asserting absolute invariability, replies to two arguments that have commonly been urged against the Monroe-Kellie theory.
[4] Demonstrated by Grashey. Hill: *op. cit.*, p. 2.

of the cerebro-spinal fluid,[1] the escape is found to be either absent or diminished during sleep and mental quiescence. (5) The retina is genetically an ontgrowth of the forebrain. An examination of the retinal vessels by the ophthalmoscope shows them to be in a contracted state during sleep, while awakening is accompanied by dilatation.[2] (6) By various experiments, it has been shown that many of these areas, whose blood supply stands in reciprocal relations to the brain, are congested during sleep, or that a derivation of blood to them produces somnolence. (7) The arterial pressure decreases during sleep. The pulse rate is slackened. The frequency and force of the heart beat are lowered. (8) One of the chief causes of insomnia is a disturbance of the vasomotor mechanism. It is a general law, which, of course, may be cut across by other special laws, that whatever tends to increase the cerebral circulation, increases cerebral activity and is hostile to sleep.[3]

These facts are all well attested and are sufficient to put beyond any reasonable doubt the anæmic condition of the cortex,[4] notwithstanding the immense complexity of conditions of cerebral circulation and our present ignorance concerning them. Many writers, like Vulpian or more recently Berger and Loewy, without committing themselves to congestion, have urged objections against cerebral anæmia. These objections are all founded upon insufficient observations or insufficient knowledge of the experimental work of others. No sleep theory that pretends to anything like completeness can afford to slur over these facts or attempt to pass them by without explanation. The great point of controversy, in the past, has been as to whether anæmia is the cause or the result of the physiological condition of the nervous system during sleep. This question is not answered by mere appeal to the fact as established by manometer, sphygmograph, and plethysmograph records, that vascular changes occur prior to the onset of sleep. So also do changes in respiration, and in muscular tone. A search for the cause of sleep has led in our own case, and we believe must necessarily lead, beyond the circulatory system and the particular nervous elements directly connected with it, to alterations occurring in the higher nervous centers,—the histological modifications of the cortex

[1] Thomson, Hill and Halliburton, 1899.

[2] Hughlings-Jackson: 1863.

[3] For a summary of experiments and observations upon insomnia, see Manacéïne, Chap. II. This law is founded upon a wide factual basis.

[4] We leave the question of cerebral venous anæmia open. The question can have no bearing on the anæmia theories, for venous congestion, if it occurs, can only be regarded as a compensation for circulatory changes, never in the sense of the older congestion theories as a cause of sleep.

and the deeper lying chemical changes that occasion them. The shutting down of the circulation is only one in a cycle of events. It results from a temporary derangement of the nervous mechanism, and in turn adds still further to the disintegration. As to the importance of anæmia as a secondary factor in the causation of sleep in man, it is yet too early to make a just estimation. In this connection, it should be remembered that the absolute quantity of blood in the brain and cord is unquestionably small: to judge from observations upon animals, it is not more than one-tenth of the entire blood in the body.[1] Such a statement, however, needs to be qualified by the consideration that it is only the cell-bodies which are well supplied with blood. We have also seen that the nerve cells are, in a certain measure, independent of the circulation. Whether or not vasomotor changes are an essential factor is a question to be left to comparative physiology.

II. The Chemical Theories.

The vasomotor theories, with which we have been dealing in the preceding paragraphs, were developed chiefly by English physiologists. Shortly after the important experiments of Durham and Hammond, researches in physiological chemistry reached a stage in development sufficient to serve as a basis for a new line of sleep theories. The principal exponents of these chemical theories are to be found among French and German writers. Naturally, their period of greatest influence did not come until after that of the anæmia theories. Largely as a matter of convenience in treatment, although not without some scientific justification, we shall divide the chemical theories into two groups: (1) the combustion theories; (2) the auto-intoxication theories.

(1). The Combustion Theories.

The common trait of the theories, which we shall treat under this rubric, is that they are all theories in terms of oxygen or carbonic acid gas. The most typical gives the name to the group. Historically, they belong to the earlier period.

In 1867, Pettenkoffer and Voit performed the classical experiments which resulted in the gaining of a new point of departure. These investigators found that the amount of oxygen absorbed during the night was greater than during the day, while the amount of carbonic acid gas eliminated was considerably less.[2] Sommer, following a year later and inter-

[1] Donaldson: Am. Text Bk., p. 736.

[2] Serious doubts are thrown upon the validity of the results of Pettenkoffer and Voit, for their tables show not only that the absorption of oxygen during sleep is greater than the elimination of carbonic

preting these results, attempts to show that sleep results from the exhaustion of reserve oxygen, which has been stored up in the cells and blood during the night for the activities of the day.

Pflüger (1875) elaborates the theory still further, and lays the greatest stress upon a gaseous exchange.[1] The stored up intramolecular oxygen is replaced by carbonic acid gas. When the replacement is complete, all the activity ceases. The intramolecular conditions which accompany the formation of carbonic acid gas are such that the atoms of its molecules at the moment of its production are in a state of most violent oscillation, just as in explosion. These explosions, which are constantly taking place throughout life, excite vibrations in the surrounding atoms, and radiate far and wide along the lines of connection of the nervous system and its annexes, causing the explosion of other cells. The molecular changes are attended by a consumption of oxygen greater than living molecules can take up at the same time. Hence, the amount of carbonic acid gas produced must necessarily diminish. Now the cortex is probably the seat of more active chemical processes than any other portion of the body, and therefore requires a large oxygen supply. As the production of carbonic acid gas diminishes, the explosions become less numerous and the condition of relative cerebral inactivity—sleep—results. The analogy of the vibrations of the strings of the harp, which continue vibrating for a long period after the blow which set them in motion, gives us a clue for the explanation of the long duration of sleep after the reabsorption of oxygen in the brain has commenced. The loss of irritability during sleep is due to the exhausted condition of the nerves and the greater cohesion of cerebral molecules, caused by diminution of the total heat produced by chemical processes in the brain. Sleep or waking depends primarily not upon the amount of potential energy in the brain, but on the amount of *vis viva* of the intramolecular movements.

The theory of Pflüger is by far the most completely developed of all this group. Various other writers have emphasized the part played by carbonic acid gas in the causation of sleep, some attributing to it a positive sedative effect;[2] but the importance

acid gas, but that it is greater than the absorption of oxygen during the waking period. The safest view is that during sleep as during hibernation there is a diminution in both the production of carbonic acid gas and the absorption of oxygen, but that the diminution in the production of carbonic acid gas is relatively greater. See Saint-Martin, Vol. CV, pp. 1124 ff. Experiments of Quinquand and Zunts. Am. Text Bk., p. 546. Manacéïne, pp. 8, 171.

[1] I abstract freely from Lancet.

[2] See Liv. Age, Vol. XCVIII, 1868, pp. 213 ff; Wurtz.

of carbonic acid gas as a positive factor has been left in the background by the line of development which the auto-intoxication theories have taken.

There is abundant evidence to prove the presence of a reserve supply of oxygen in the cells. An amœba continues movement in an atmosphere of hydrogen for twenty-four minutes; an excised muscle remains irritable for even a longer period.[1] In both cases after complete exhaustion oxygen is necessary to restore vitality.

The question of whether or not the cortex is the seat of very active combustion cannot, at present, be said to be definitely settled. Results from Mosso's[2] temperature experiments and Hill and Nabarro's[3] experiments on gaseous exchange in muscles and brain are contradictory. Pflüger is, without doubt, right in attributing to the cells of the nervous system the greatest sensitivity to the lack of oxygen. This would explain the quick and violent death of the higher vertebrates from asphyxia, in comparison with the slower death of lower organisms, since in them the nervous system has gained a more complete control of the respiratory and cardiac muscles. The other cells, in particular the ciliary cells, continue to function long after the nerve cells have ceased.[4] Speck (1892) has performed an important experiment, directly to the point. He inhaled air from a vessel, counting at the same time. The air lost its oxygen. When the oxygen of the inhaled air fell to eight per cent. of an atmosphere in pressure, the counting stopped and unconsciousness resulted, although the other functions of the body showed no alteration. Recent investigations have brought out fundamental facts concerning tissue oxidation, and have exhibited at once the great complexity of the chemical processes occurring in the cell and our immense ignorance of them. "The amount of oxidation is not increased in an atmosphere of pure oxygen nor within wide limits is it affected by variations in atmospheric pressure."[5] A certain amount only of oxygen is needed, and this amount is determined by the amount of metabolism, not the reverse as was formerly supposed.[6] As to the cause of cell decomposition, we have evidence that certain bacteria, chiefly in the intestinal tract, cause putrefaction, but as to the main cause we can only say that it is internal, in the cell itself, and resembles fermentation. The function of oxygen appears, then,

[1] Verworn: p. 263.

[2] Mosso, 1894, finds the temperature of the brain frequently higher than that of the aortic blood.

[3] Hill: 1896, pp. 152 ff.; Hill and Nabarro, 1895, find combustion of muscles very much greater than of brain.

[4] Verworn: *loc. cit.*

[5] Lusk: Am. Text Bk., p. 945.

[6] See Loeb, 1899, p. 165.

to be simply the oxidation of injurious decomposition products. With our present meager knowledge it would be hazardous to attempt any definite statement in regard to the correlation of mental activity with the amount of oxidation in the cortex, and entirely unwarranted to attribute sleep to such a simple factor as the lack of oxygen (Sommer)[1] or decrease in gaseous exchange (Pflüger). However Pflüger's conception of sleep or waking as dependent upon the *vis viva* of chemical processes, provided *vis viva* is interpreted to mean both a certain intensity and extensity of cortical activity, is a profitable one.

(2). The Auto-Intoxication Theories.

The common starting point of auto-intoxication theories is the influence of certain products of decomposition of living substance upon the continuance of cell activity. These products act not merely catalytically, but, as the name auto-intoxication implies, have a decided and positive effect upon metabolism.

Obersteiner (1872) was the first important advocate of the theory that the cause of sleep is to be found in the accumulation of acid products in the brain. Previously, the acidity of the cortex in fatigue and sleep had been noted. Obersteiner laid especial emphasis upon lactic acid. The condition of the circulation, although secondary, he admitted to be of great importance, since upon it depended the removal of the fatigue products.

Preyer (1877), through the weight of his name, gave wider currency to the theory.[2] He first distinguishes sleep from allied pathological states by the fact that normal sleep is always preceded by some fatigue of muscle, sense organ, or brain. The condition of mental activity is a certain amount of oxygen. "Now as the brain of a sleeping animal receives as much blood as it does when the animal is awake, we are compelled to infer that the influence of oxygen on the waking and sleeping brain is different." This must be due to the accumulation in the blood of such fatigue products as lactic acid and creatine. A reduction of the amount of oxygen available for cell activity results from the great affinity of these substances for oxygen. We have, then, three well defined and causally connected stages: (1) fatigue due to the accumulation of certain decomposition products; (2) sleep, an intermediate state; (3) awakening, resulting from the complete oxidation of the fatiguing substances.

[1] Foster has pointed out that on the exhaustion theory it is necessary to explain why the respiratory centers are not stimulated to greater activity, as a compensation, by anæmia. Foster, 1891, Part IV, p. 415.

[2] See Preyer, Med. Examiner, 1877.

The auto-intoxication theory cannot be held in the form stated by Preyer, for it rests upon two assumptions: (1) that the presence of oxygen is the essential condition of mental activity, and (2) that the circulation remains unaltered during sleep.

Rachel (1883) offers a theory in many respects more completely worked out in detail than Preyer's, and somewhat less objectionable. He uses facts from experiments on muscle fatigue to show that activity may cease from the action of fatiguing substances, notwithstanding the presence of material available for metabolism. From the partial independence of the cell from the blood supply, he contends that the purifying function of the blood is of more importance than its oxygen-bearing function. Sleep results from the fact that the capacity of the blood supply for elimination of fatigue products is limited. The direct cause is a surplus of such products, accumulated from all portions of the body. Secondary factors are found in a diminution in amount of intramolecular oxygen and in a decrease of intravascular pressure, not necessarily followed by a pronounced anæmia in the capillaries. Rachel differs from Preyer in holding that the fatiguing substances are already oxidized, and does not attempt to trace just how they affect cell metabolism.

The more recent auto-intoxication theories show clearly the influence of the development of the science of bacteriology and the investigations made upon animal poisons. The epoch making work of Selmi on cadaveric poisons did not appear until 1870. He gave the name of ptomaines to the transition products in putrefaction. They are basic in character, and are formed by the action of bacteria upon organic matter. Brieger restricts the term ptomaine to the non-poisonous basic products, while he called the poisonous products toxins.[1] In distinction to the ptomaines are the leucomaines, also basic in character, but the results of cell decomposition, without the action of bacteria.

It is the fatiguing and narcotic action of many of these leucomaines that serves as the point of departure for the sleep theory of Errera. These substances are formed more rapidly than they can be oxidized, and being carried along by the blood stream, are retained by the cerebral centers in sufficient quantity to produce sleep. During sleep the leucomaines are oxidized, and the oxidation products, having no special affinity for the cortical cells, are carried away by the blood. Hence, for Errera as for Preyer, sleep is only one stage in a more or less rhythmic cycle. Insomnia due to excessive fatigue is produced by the differing effect of the larger quantity of toxic substance.

Berger and Loewy (1899) have lately argued to the same effect.

[1] Brieger: Ueber Ptomaine, Berlin, 1885–86.

They, however, have seen the necessity of completing the chemical explanation by a histological one, and have refused to limit the action of the narcotic substances to any one portion of the nervous system.

We are now ready to discuss in detail the more important evidence upon which the auto-intoxication theories rest.

Preyer made many attempts to produce fatigue by the injection of lactic acid, with very variable results.[1] Ranke was more successful in the use of a solution of beef broth with a greater variety of fatiguing substances.[2] Mosso, by the injection of the blood of a fatigued dog into the circulation of an active one, was able to induce complete symptoms of fatigue.[3] Mental derangement and cases of mental disorders during infectious diseases show a close correspondence between the psychological state and the presence of poisonous and convulsive substances in the body.[4] Perhaps, the most important evidence of all comes from the experiments on the toxicity of the urine, first exhaustively studied by Bouchard. Bouchard's experiments were performed by collecting the urine of three different periods of the day (7.15 A. M.–3.15 P. M.; 3.15–11.15 P. M.; 11.15 P. M.–7.15 A. M.).[5] After neutralizing and filtering, the fluid was injected into the veins of the animal. He found that, although the urines of sleep were more rich in solid matter, in equal volumes they were almost always less toxic than the urines of the day.[6] The difference between the two urines is further brought out by the fact that the one is antagonistic to the other. The total uritoxy of a mixture of equal quantities of both urines is less than the sum of their uritoxies.[7] By the help of charcoal acting on the urine so as to separate its constituents, seven distinct toxic principles were found:[8] (1) a diuretic substance—urea; (2) a saleogenous substance; (3) one that contracts the pupils; (4) one that lowers the temperature; (5) an organic convulsive substance; (6) a mineral convulsive substance—potassium; (7) a narcotic substance. This narcotic substance was fixed, organic, not fixed by carbon, soluble in alcohol, and found in alcoholic extract with urea and other substances. This substance has not yet been chemically analyzed, and hence it is named only from its physiological effect. In sleep, the urines are always markedly convulsive, while those of the day period are very little or not at all convulsive, but produce narcosis. In a passing remark concerning the auto-intoxication of sleep, Bouchard suggests that sleep may be due to the accumulation of these narcotic substances, while awakening is due to that of the convulsive substances.[9] Experiment upon repose after great muscular exertion in the open air shows a diminution in toxicity by nearly one-third, both during the period of exercise and that of rest. Bouchard concludes that the low toxicity is the result of the more complete oxida-

[1] Preyer: *op. cit.*
[2] Ranke: Archiv. f. Anat. u. Physiol., 1863, p. 422; 1864, pp. 320 ff.
[3] See Donaldson, Am. Text Bk., p. 740.
[4] See Oliver, in Introduction to Bouchard.
[5] Bouchard: pp. 36 ff.
[6] The ratio of 7:5:3 held for the different periods.
[7] The uritoxy is the unit of measurement, first employed by Bouchard. It is the toxic amount necessary to kill a kg. of living substance.
[8] Bouchard: p. 262.
[9] Bouchard: p. 41.

tion of organic substances during muscular activity. This might be used to explain the disturbance of sleep, following excessive fatigue, since the organic narcotic substances would be decreased through oxidation, while the mineral convulsive substances would not be affected. Investigations upon the toxicity of the blood have even a more direct bearing on sleep problems than those upon urine. Bouchard's estimate from his own experiments is that one kilogram of blood can kill between 1,250–3,000 grams of living tissue.[1] This, he admits, is perhaps too high an estimate. However, death in an animal results from increase in the amount of poison in the blood to two and one-half times its normal quantity.

We have already pointed out the danger of interpreting a physiological by reference to a pathological condition. Arguments from the effects of drugs and narcotics are precarious, so also arguments from Bouchard's experiments, for, in all, urine was injected until death of the animal followed. The mental state produced prior to death was that of stupor, not sleep. Yet, inasmuch as toxic substances are shown to result from functional activity, there is a strong probability that under normal bodily conditions their accumulation plays a part in the causation of sleep. They may act physically, *e. g.*, by mere clogging, as well as chemically.[2] To assume that auto-intoxication is the sole cause of sleep, or to attribute the narcotic effect to any one group of decomposition products, is to dogmatize. "We really know only that living substance is continually undergoing decomposition, for this is apparent from the output of decomposition products. But as to the path from the complex proteid compounds to the end products, as to the special chemical transformations that take place, our knowledge is very incomplete, since, as yet, the composition of proteids is known very slightly."[3] On the auto-intoxication theory, notwithstanding Errera's attempt, it is extremely difficult to explain the long duration of sleep.[4] An insufficient supply of nutrition, in the end, leads to the same results as an accumulation of decomposition products. In all normal fatigue curves the loss of power is at first rapid and then slow.[5] These facts suggest that at the beginning of sleep the more active factor is an auto-intoxication and that, when the oxidation process of the fatiguing substances is completed, the intensity of sleep sinks and remains for so long a period at low level, in order to allow the cells to recover from the effects of exhaustion of the day and to lay in a store of new materials. Thus, exhaustion as well as an accumulation of fatigue products would precede sleep. Both would be causally connected with its onset. The exact relation between the two, of

[1] Bouchard: pp. 69 ff.
[2] Loeb: p. 165, 1899.
[3] Verworn: p. 161.
[4] *Cf.* Howell, p. 338.
[5] Donaldson: 1897, p. 312; p. 322.

course, needs working out, but there is no valid reason for singling out, as the auto-intoxication theories do, only one of the two factors that produce fatigue, to the exclusion of the other. Concerning the relative importance to sleep (in man) of the decomposition products accumulating in the nervous tissue from inadequate removal and those that are imbibed from the blood stream we are also in the dark. There is no way at present of determining. The direct accumulation of waste products, checking the activity of the cells that produce them, is the more fundamental of the two, since it occurs in the absence of blood circulation.

The chief criticism of all the various chemical theories considered we have found to be a lack of adequate experimental basis. What are we to say of the possibility of a chemical explanation of sleep? It is the aim of physiology to bring vital phenomena under the same physical and chemical laws that have been established in the inorganic world.[1] Although physiological chemistry is tremendously hampered at the outset by the fact that an analysis of living tissue is impossible, there is no sufficient reason for thus early giving up in despair or returning to vitalism. Progress must necessarily be slow and labored. We have unequivocal evidence to show that the chemical composition of the fatigued nerve cell,[2] whether the fatigue be produced by artificial stimulation or as the natural result of a period of activity, is different from that of the rested cell. If the ultimate explanation of the phenomenon of sleep is to be found anywhere, it must be sought in the chemical composition and the chemical changes occurring in the nerve-cell. The work so far done gives us hope that, if not a complete explanation, at any rate a more complete than any yet given may be forthcoming. In the meantime it is the part of wisdom to avoid any too hasty or too ambitious theorizing that will tend to limit the scope of investigation.

One objection that has frequently been urged against the chemical theories so far has never been satisfactorily answered. Monotonous repetition of a stimulus or reduction in the number of adequate stimuli may produce sleep without the presence of fatigue. We shall reserve a consideration of this objection until we come to treat of sleep from the evolutionary standpoint. From any other point of view a full answer is impossible.

III. The Histological Theories.

The great improvement in microscopical apparatus and technique, together with the discovery of new histological methods,

[1] *Cf.* Verworn, Chap. I.
[2] See Chap. III.

within the last decade has opened up a new and attractive field to science. The outlines of the nerve-cell and its processes, brought out with clearness, show the neurocyte [1] to be a structural unit. With the recognition of the morphological independence of the nervous elements, one of the main problems for the nerve histologist is to account for physiological interdependence. Hence, many painstaking investigations have been made upon the difference in condition of the neurocyte during functional activity and during repose. These investigations have a direct bearing upon the problem of sleep, and have resulted in the formulation of numerous sleep theories.

The first of these theories to deserve attention is that of Rabl Rückardt (1890). The conception that underlies his theory is that the neurocytes possess a kind of amœboid movement, which allows them to make or break contact by means of a retraction or expansion of the prolongations of their neuro-dendrons. Sleep and hypnosis are the psychological correlates of a partial paralysis of these amœboid prolongations, resulting in an isolation of nervous elements. Lepine (1894), in attempting an explanation of anæsthesia and motor paralysis in hysteria, is led to a somewhat similar theory of sleep. He confines the amœboid movement to the extremities of the neurodendrons. Querton may also be quoted in support. Duval's theory (1895) is by far the most widely known and elaborated of any of these theories. Wiedersheim's alleged direct observations of amœboid movement in the neurocytes of the superior ganglion of Leptodera hyalina have largely influenced him towards amœboidism. He does not regard actual contact as essential for transmission of nervous impulse, but only a certain degree of contiguity. During sleep, this degree of contiguity is lost by a retraction of the ramifications of the cell-processes. He explains the functional activity of the lower centers during sleep, by the fact that currents of contact are set up among the amœboid prolongations by chemical processes started by decomposition products (chemiotropism). Chemiotropism is not intense enough to allow the impulse to reach the cortex. When the necessary degree of chemiotropism is reached and the currents of contact have become sufficiently extensive, awakening results.[2]

There remain but two other histological theories to be considered. Since they are both largely the result of negative criticism, it might be well here to attempt a brief summary of the most important facts discovered concerning the neurocyte in functional activity, quiescence, and fatigue.

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[1] Terminology of Fish.

[2] Pupin (1896) strongly defends Duval.

1. As to cell-body.

Flesch (1884) noted the difference in the reaction of cells to staining reagents after activity, and distinguished cells on this basis as chromophile and chromophobe. Vas (1892) experimented upon the cervical ganglion, and confirms Flesch. Vas found that the immediate result of activity was a swelling of the cell. Mann (1894) extended the observations to motor cells of the cord and sensory cells of the retina of the dog. He concludes that during rest there is a storing of several chromatic substances, which are used up in activity. In the cells observed there was in normal activity an increase in the size of cell, nuclei and nucleoli. Fatigue was characterized by a shrinking of the nucleus and probably of the cell and by the formation of a different chromatic substance. Lugaro (1895) in the main confirms Mann. The decrease in volume has been put beyond doubt by the thoroughgoing investigations of Hodge (1892-94). He found the most clearly marked differences in the nuclei, the decrease depending upon the length of time of stimulation. The outlines of the cell and nucleus became irregular, and vacuolation was present. Hodge also demonstrated the presence of fatigued cells in various animals after a day of normal activity. Further experiments made by the same investigator upon the effects of old age showed likewise a decrease in the volume of the cells and nuclei and an increase in pigmentation.[1] Heger (1899) found a shrinking of cell-body in ether, chloroform, and morphine narcosis.

2. As to cell processes and appendages (gemmulæ).

Heger has shown that in animals decapitated in the waking state, under normal conditions, the neurocyte possesses numerous dendrites of uniform calibre throughout their whole length, provided with many gemmulæ. The appearance differs somewhat from one species to another, but remains the same in animals of the same species. Under the action of chloroform, morphine, alcohol, and prolonged electric stimulation, Demoor (1899) noted the loss of gemmulæ and the formation of moniliform varicosities, which disappeared on return to normal state. Experiments of Stefanowska, Querton and Heger, confirm the observation. The results of Lugaro's experiments in the main agree.[2] He is convinced from his own and Ramon y Cajal's experiments that many of the varicosities observed are attributable to defective technique. The formation of these varicosities he regards as occurring independently of the retraction of gemmulæ, and as an indication of fatigue. He found little alteration in the condition of the trunks and larger branches. Berkeley[3] has shown that the gemmulæ are irregular and absent in certain mental disorders. After numerous experiments upon normal, over-excited, hibernating, narcotized animals, and animals killed by cold, Heger[4] concludes that variability is an important property of the neurocyte, and that these variations can occur in the cell-body, the prolongations, or the gemmulæ, simultaneously or independently. Hodge[5] has extended these investigations to normal fatigue, with similar results. During the growth of the brain, while medullation of fibres has not taken place extensively in the cortex, mass movements of cells to gain their position in the adult structure

[1] Hodge: Jour. of Physiol., 1894.

[2] Lugaro: 1898.

[3] See also Obsteiner, Die nervösen Centralorgane, Leipzig, 1888, pp. 112 ff.

[4] Heger: *op. cit.*

[5] Hodge: Amer. Jour. of Physiol., II, No. 3, p. 13.

doubtless can occur. Notwithstanding the seeming positiveness of these results, the question as to whether or not any movement occurs in the developed neurocyte at all comparable to the movements of the amœba or leucocyte must be regarded as still open, so long as Kölliker and Ramon y Cajal refuse to give their assent.

Ramon y Cajal's refusal to accept amœboidism is due to his belief in the great mobility of the neuroglia cells, in which the neurocytes are bedded for support. This forms a starting point for a theory of sleep.[1] The neuroglia cell by an intervention of its pseudopodia between the neurocytes, he supposes, can block or stop the passage of nervous impulses, so that various degrees of nervous coherence are possible. Experiments have confirmed the mobility of the neuroglia cells.

Lugaro (1898), accepting the plasticity of the gemmulæ, presents an entirely original theory. According to him, in normal mental activity only a few of the possible connections between neurocytes can at a given time come into play. It is necessary that the rest be interrupted by a retraction of gemmulæ in order to impede access of other stimuli, which would be able to deviate or suppress the one that is being elaborated in the cell. Strong stimuli or those of immediate importance to the well-being of the organism can, of course, break through. With the exhaustion of the contractility of the gemmulæ due to fatigue (auto-intoxication in particular), greater torpor of their movements results. Consequently, contacts are multiplied until the nervous impulses become more and more diffused throughout the cortex and individual processes are lost in the maze. The same condition can be reached through a lack of stimuli. Lugaro repeatedly appeals to psychology to support his theory, particularly to the phenomenon of attention. Wundt's[2] is by far the most satisfactory psychophysical theory of attention. It possesses innumerable advantages over Lugaro's. As an explanation of the cortical state during sleep and dreams, Lugaro's theory is seen at its best. But dreams are only one among many abnormal, or better non-normal mental states, which are characterized by a disaggregation of the normal consciousness into smaller and more elementary groups.[3] Dreams give the type of the greatest dissociation. If psychological facts are to be urged in behalf of histological theories, their weight would seem to be in favor of that of Duval or Ramon y Cajal. A compromise between Duval's and Lugaro's theory is not, however, an impossibility.

It is hardly within the province of a layman to attempt de-

[1] Ramon y Cajal: 1895.

[2] Wundt: 1887, Bd. I, pp. 282 ff; G. E. Müller's theory is also well known, Zur Theorie der sinnlichen Aufmerksamkeit, 1873.

[3] *Cf.* Janet, L'Automatisme psychologique, 1894, pp. 484 ff.

tailed criticism of histological theories. From a glance at those presented, it will be seen that three lines of attack, and the only three lines possible, have been taken: (1) a dissociation of nervous elements, caused by an amœboid movement of the attachments of the neurocyte; (2) a dissociation of nervous elements, caused by an interposition of the pseudopodia of other cells; (3) a diffuse connection of nervous elements caused by torpor of movement of the attachments of the neurocyte. The decision between these three must be left to future investigations of the histologist. It is no reflection on the importance of such research to admit that the histological theories can only be theories of the changes occurring in the nervous mechanism. The causes of its derangement will still have to be sought.

IV. The Evolutionary Standpoint.

In our consideration of the various lines of sleep theories we have found that no one of them alone is adequate as a complete explanation. The vasomotor, the chemical, the histological theories are all capable of being based upon a wide range of facts. Their several claims cannot be ignored, but must be reconciled. In the immense complexity of the human organism, the primary factors of sleep are so overlaid and obscured by secondary ones that it is next to impossible to trace them out. Hence the necessity, if profitable work is to be done in the future by the physiologist, for a broader point of view. The sleep problem must be attacked genetically. It is true that comparative physiology is still in its infancy, that at present few facts are known concerning sleep phenomena except in the higher vertebrates. To attempt any elaborate theorizing would be useless. There are, however, enough facts to point unequivocally to the conclusion that sleep is the product of evolution, and to indicate the main lines which any evolutionary theory will have to follow. Three questions, which cannot be kept wholly separate, naturally arise.

1. What is fundamental in the phenomena?
2. How has selection operated upon sleep? How have the secondary factors crept in, and what is their relative importance?
3. How shall we define sleep? What are the limits of the problem?

Hodge and Aikins (1895) have made a careful study of the daily life of a protozoan, with special reference to the rhythm of rest and activity. Observations were recorded upon a vorticella, for a period of twenty-one hours, without interruption. Thirteen other experiments were afterwards made. Automatic contractions of cilia were continuous, those of the vesicle

nearly so, while contractions of the stalk were irregular and occurred usually upon presence of stimuli. The conclusion to which the writers are led is that vorticellæ neither rest nor sleep. Hodge assumes that the unicells possess a rudimentary form of consciousness. Whether or not the lower organisms do now or have once possessed consciousness, which has since dropped out, is a disputed question. It would be unwise, before there is a more general consensus of opinion among authorities, to encumber a sleep theory at the outset by definite commitment to any theory of the origin of consciousness. These experiments with the vorticellæ are of great value, since they show clearly, what might be expected *a priori*, that in a simple organism with adequate provision for food supply and removal of waste products continuous response to stimuli without diminution of irritability is possible. There is no reason to hold that fatigue is a general phenomenon common to all life.

For the sake of making the problem of the fundamental in sleep more definite, let us try to picture what would be the mental state of the simplest organism capable of serving as the support of consciousness, and living under conditions so favorable that fatigue could not occur. This primitive consciousness we may, without violence, suppose to be a motor consciousness. If we exclude the action of hostile agencies in the environment, the only occasion for the cessation of consciousness would be the lack of adequate stimuli. A state of full consciousness[1] would exist in the presence of an adequate stimulus, and on its absence a mental blank or a vague organic sensation. At irregular intervals states of consciousness and unconsciousness would succeed each other. The ultimate reason for the presence of the latter is not to be sought outside of the organism in the withdrawal of stimuli, for stimuli are always present, but in the internal conditions which render the organism unable to receive or respond. The chemical composition of the cells is relatively too simple, the nervous elements too poorly organized, or the vascular system, if blood circulation be present, defective. The operation of these causes is not confined to the lower animals. Strümpell[2] reports a case of general anæsthesia in a boy of sixteen, who was left with the sensibility of only one ear and one eye unimpaired. Sleep could be produced at any time by the closure of the eyelid and the stoppage of the ear. Through an inherent limitation of capacity, other than that manifested in or brought about by fatigue, the physiological processes underlying consciousness may sink to so low a level of intensity and extensity that

[1] Idea or sensation given in a state of attention and felt. *Cf.* Titchener, Outline of Psychology, New York, 1899, pp. 249 ff.

[2] Strümpell: Pflüger's Archiv, Bd. XV, p. 573; Nature, Dec. 13, 1877 (tr.).

sleep results. This inherent limitation of capacity is to be conceived of as due to a state of development inadequate to meet the demands of continuous consciousness. We shall include all the foregoing causes as well as those that spring from degeneration under the rubric Lack of Development.

The factor, Fatigue, now demands our attention. Even without the presence of consciousness, the development of the multicellular organism must have continued to the point where a fatigue of nervous elements would occur, for, with increasing complexity of structure and function, the utility of bringing the cells and groups of cells into more intimate relations with each other, in order to gain unified co-operation and advantageous adaptation to environment, becomes apparent. The performance of this function calls for a developed nervous system. The ascendency of nervous tissue over all other tissues is to be correlated with an increase in chemical complexity of the cell and an increased metabolism. For its demand upon food supply and for removal of waste, the nerve cell is left dependent upon the alimentary tissues and the circulatory system. Fatigue, implying among other things a diminution of irritability, thus inevitably arises in the course of development. If such a condition would be brought about without the presence of consciousness, its onset is made all the more certain and rapid by the possession of mentality, for consciousness once present has a survival value and adds greatly to the demands made upon the organism. Were it not for fatigue, the development of the nervous system might be carried to such a point that consciousness could be present continuously. Fatigue is the one great factor that forever makes sleep a vital necessity. Arising in the course of development, it ends by limiting the possibilities of development. Operating as a cause it limits further capacity for function, though it, itself, results from a limitation of capacity. As such it can be placed along with the other causes under the rubric Lack of Development. But Fatigue is a positive, well defined, wide spread condition arising only after exercise of function. It can be clearly distinguished from the other conditions inhering in the organism that limit capacity; and since the distinction is an important one and we have no other term to use, we shall confine the term Lack of Development to those causes other than fatigue.

Sleep, then, results from the limited capacity of the organism to receive and respond to stimuli, either through Fatigue or through Lack of Development. Both factors are internal. The relation of each to function can be traced along chemical, histological and vasomotor lines. What is their relative importance in the causation of sleep? In man, fatigue by itself can occasion sleep, while a reduction of external stimuli to the

minimum is not sufficient to cause sleep in an individual of highly organized and well nourished brain without the presence of fatigue; for central excitations, along with the remaining peripheral, would maintain an adequate support for consciousness. In animals low down in the scale, cessation of consciousness can occur without the presence of fatigue, by the mere withdrawal of adequate stimuli. Thus at one extreme of the series fatigue alone can cause sleep, at the other lack of development. Between the extremes the two factors do not stand in relations of reciprocal importance, for in most instances the more poorly organized and developed the nervous system, the more easily is it fatigued. This is well illustrated by the ease with which children, savages, and the insane are fatigued by work that requires mental concentration, and their great need for sleep in comparison with the normal adult. On the other hand, the short sleep periods of great men have often been remarked.

We are now ready for our second question as to the operation of selection upon sleep and the rise of the secondary factors. In every organism at all developed, we find firmly rooted habits of activity and repose. These habits are rhythmic, and, if not ultimately caused, have been powerfully influenced by rhythmic changes in environment. Even without the presence of fatigue, such changes would have been capable of establishing rhythmic periods of greater and lesser activity; but, fatigue being an inevitable product of evolution, it becomes all the more imperative that rest periods be grouped. It is an obvious economy to the organism that the rest periods should correspond to periods of lessened adequate stimuli. A very profitable field is open to the physiologist in tracing out this correlation. Loeb has already shown the importance of light to animal life. Heliotropism,[1] quite comparable to that in plants, is observable in the animal kingdom. The influence of light upon sleep habits[2] is clearly brought out by the fact that animals which depend chiefly upon smell and hearing are much less regular than those with largely developed vision, such for instance as birds. The former can sleep quite independently of the time of day, while sleep in the latter corresponds closely to the rhythm of daylight and darkness, even varying with the changes of season. Lack of data compels us to leave the most fascinating problem of sleep rhythms in this fragmentary way.

With the development of the organism and the appearance of new adaptations, an opportunity for the operation of new internal factors is afforded. The most important of these is the blood supply. That the circulation is not fundamental can

[1] Loeb: 1890.
[2] Donaldson: 1897, p. 297.

be seen from the fact that in insects and plants, devoid of a vascular system, well defined periods of rest and activity occur.[1] When the organs of blood circulation appear, according to the principle of utility their development is accompanied by an increased control of the nerve cells over the supply. A complex and nicely adjusted vasomotor mechanism is the result. The rhythm of this system is derived from the rhythm of the vasomotor nerve cells. Their rhythm in turn is not independent of, but directly determined by, the primary rhythm in the central nervous system, so that while the higher centers are made dependent upon the circulation for food and removal of waste, they are dependent upon it as a master upon the performance of the work of a servant, not as a servant upon the bounty of a master. The precise work that the circulation performs in bringing about the condition of sleep in man is probably rightly estimated by Howell,[2] who urges that diminution of blood supply can best explain the sudden and comparatively simultaneous onset of sleep.

High up in the animal series, where consciousness plays an important role, another factor enters,—conscious adaptation to the conditions most favorable to sleep. A glance at the arrangements of modern sleeping rooms, the preparations usually made before retiring, and the bodily position assumed for the night's repose, will show that they have as their objects the reduction of external stimuli to a minimum and the derivation of blood from the head. Adaptations originally conscious may, of course, become reflex and appear later as inherited reflexes.[3]

There remains but one other factor to be considered. The psychophysical phenomenon of attention cannot be overlooked.[4] The hypnotist in artificially producing sleep resorts to a sudden stimulus or repetition of monotonous stimulus, frequently a command or suggestion, capable of holding the attention. A complete sleep theory should seek to trace the factors exhibited in the artificial state as they occur in the natural state, and to show their relative importance to sleep phenomena in general. Hypnotic sleep is most easily explained physiologically by inhibition. Certain processes on their arousal inhibit other processes in the cortex, reducing them below the level of extensity required for consciousness. It is possible that fatigue, produced by excessive activity of portions of the cortex,

[1] Loeb: 1898.

[2] Howell: 1897.

[3] In this connection Goltz' experiments are of interest. His decerebrized dog "slept" like any normal dog. Many of the habitual positions in sleep might well be purely reflex; see Goltz, Der Hund ohne Grosshirn, Pflüger's Archiv, Bd. LI, 1892.

[4] *Cf.* Külpe, Outlines of Psychology (Tr.), 1895, pp. 452 ff.

may also contribute powerfully to the result. The influence of repetition of monotonous stimuli upon sleep has often been attributed wholly to fatigue, but in our judgment it more properly falls under the same general explanation as hypnotic sleep. We must deny to these causes fundamental importance to the production of sleep, for their operation is accidental and without universal significance. The nervous mechanism is not so poorly constructed that under normal circumstances it is obliged to suspend its chief function from an antagonism of parts.

In a work that is admirable for its array of facts, Madame Manacéïne has attempted to state a theory of sleep in the brief formula: "Sleep is the resting period of Consciousness."[1] The phrase is not intended as a metaphor, but is put forward seriously as an explanation and continually used as such. There is probably no field in science, where the loose use of terms is more harmful than in psychophysics. The formula as it stands is meaningless nonsense. Consciousness, as such, has no more need for rest than it has for nutrition. It is true that the sleep problem has a psychological as well as a physiological side. Investigations of hypnagogic states and of dreams are to be correlated with investigations of the condition of the brain. Between the two series, no causal relation can be assumed. But just as the *raison d'être* of death is to be sought in a breaking down of the physical organism, so the *raison d'être* of sleep is to be sought in a temporary derangement of the nervous system. Manacéïne's formula, when put into scientific language and properly interpreted, is a profitable conception. Sleep is the resting period of the *support* of consciousness. This differentiates the phenomenon of sleep from all other rhythms, and gives the sleep problem a definite place under the more general problem of rhythms in the nervous system. The term *sleep* is then reserved for that particular phase of the rhythm of the cortical or nerve cells which has as its psychological accompaniment a cessation of consciousness. It is well that such a differentiation should be sharply made. The nyctitropic movements in plants, the rhythm of activity and repose in a decerebrized dog or (if consciousness be denied to them) in the invertebrates, are only comparable to sleep on its physiological side. Without the psychological accompaniment, the term is no more applicable here than it would be to all periods of loss of power in the diurnal fatigue rhythm.[2] A word perhaps needs to be said concerning the various states that resemble sleep. In some cases it may be difficult to determine; but as the conditions of sleep become more fully known, it will become

[1] Manacéïne: pp. 59 ff.

[2] For curve of diurnal rhythm, see Lombard, Jour. of Physiol., 1892; Ostanikow and Gran, Neurolog. Centralbl., 1893.

easier to distinguish between the normal and the abnormal. Little light upon the sleep problem can be expected from a study of abnormal states. Such a study demands first a thorough understanding of the normal, and is rather a field for the application of general principles already discovered to special problems, than a source of new knowledge.

The three questions raised at the outset have been but meagerly and imperfectly answered. It is enough to have pointed out some of the difficulties and the possibilities that lie before an evolutionary theory of sleep.[1]

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Manacéïne at the end of Chap. I has an excellent bibliography. She also gives a short account of many sleep theories (pp. 40 ff), although with little attempt at criticism. I take pleasure in acknowledging my indebtedness to her work for much of the purely historical part of this article.

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[1] Besides the various theories we have treated, there are local theories of sleep; see Manacéïne, pp. 40 ff., and purely psychological (and mystic) theories. Their defects are so palpable that, with limited space, we have not thought it worth while to consider them. For typical theories, see Binns, Bigelow.

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